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DETERMINATION OF THE RADIOCHEMICAL PURITY OF ^{51}Cr-EDTA

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ABSTRACT

The miniature chromatography systems were elaborated to determine the radiochemical purity of chromium ^{51}Cr-EDTA.

Chromatography results using four different solvents were obtained and studied. We conclude that 33% W/V aqueous solution of ammonium sulphate pH 7,5 gives the best chemical separation and we recomend it as the solvent of choice for chromatographic separation of ^{51}Cr-EDTA.

DETERMINAÇÃO DA PUREZA RADIOQUÍMICA DE ^{51}Cr-EDTA

RESUMO

Determinou-se a pureza radioquímica de ^{51}Cr-EDTA por meio de um sistema de cromatografia miniaturizada. Obtivemos e estudamos resultados cromatográficos usando 4 solventes diferentes. Concluimos que a solução aquosa de sulfato de amônio 33% P/V pH 7,5 apresentou separação química adequada e a recomendamos para separação cromatográfica de ^{51}Cr-EDTA.

INTRODUCTION

The non radioactive gold standard for measurement of the glomerular filtration rate (G. F. R.) in renography was inulin. It is a fructose polimer of about 5000 molecular weight. Inulin clearance is the best measure of glomerular filtration rate, but its estimation by chemical methods was laborious. Because of these factor, a number of agents labeled with radioactive tracers was introduced for this measurement. Metal complexes of ethylene diamine tetraacetic acid (EDTA) was used for this purpose. Since its introduction by Garnetts, Parsons and Veall in 1967[4]. ^{51}Cr-EDTA provides a convenient substitute for inulin. Its clearance is practically identical to that inulin[2]. ^{51}Cr-EDTA was used as reference for other preparations[1].

Almost all the papers that deal with ^{51}Cr-EDTA discuss their medical aspects.

From the point of view of diagnostics the radiochemical purity of the preparation is of major importance.

Our objective was to cover their radiochemical problems. Chromate and chromic ion were considered to be the likely contaminants of chromium preparations. It was intended to use miniature chromatographic procedures for the determination of the contaminats[3,5].

The advantage of this method is that the radiochromatographic systems are chosen such that in one the impurities move with the solvent front (Rf = 0.8 - 1.0) while the radiopharmaceuticals remain near the origin (Rf = 0.0 - 0.3) or vice versa. This permits one to cut the strips at Rf=0.5 (midway) and to assay the two segments to determine the level of radiochemical impurity in the preparation.

Utilizing paper and specific solvent systems it is possible to resolve and quantify radiochemical components within a radiopharmeceutical based upon distinguishable migration along the chromatogram.

We had two propositions for the present study. One of them was to choose the suitable solvent for the development of the chromatograms. The other one was to establish the possibility of substitution of the time - consuming standard method (conventional paper electrophoresis) for quality control of ^{51}Cr-EDTA by a rapid, reliable and inexpensive method such as miniaturized chromatography system.

A critical point in the quality control of radiopharmaceuticals is the time available.

This report outlines the method used in our laboratory for quality assurance of ^{51}Cr-EDTA.

MATERIAL AND METHODS

Solvent optmal for the determination had to be established in the first place.

The solvent: The selection of a solvent material for a separation is almost entirely an empirical procedure. In most instance the solvent consists of an organic liquid containing some water and, in many cases also acid such as hydrochloric acid or a salt.

The paper: Whatmann 3MM has been a good chromatographic paper. The flow rate results in a rapid, but no so fast separation.

The miniaturized chromatographic procedures were performed using Whatmann 3MM paper (1 cm x 6,5 cm) as support with four different solvents (ethanol: concentrated HCl: water 50:25:125; ethanol: water: concentrated ammonia solution 2:5:1; ethanol: water 60:40 and 33% W/V aqueous solution of ammonium sulphate pH 7,5; called 1-2-3-4 respectively).

The paper was spotted a 1 cm from the bottom. The strips were placed in a vial containing aproximately 1 ml of each solvent.

Preliminary scanning indicated, on the basis of the radioactive measurements, that the impurities remained at the origin while the labeled EDTA migrated with the solvent front.

The chromatogram was developed for a distance of 5 cm. After developing the strips were then removed, dried and may be cut midway (section 1 and section 2) between the origin and solvent front portions and each piece counted in a well-type scintillation counter (ANSR gamma counter ABBOT LAB) with a 200-500 KeV window.

This scanning is advisable if the strips are cut between the two peaks. The activity of each portion was compared with the total radioactivity of the strip.

RESULTS AND CONCLUSIONS:

All solvents tested give good separation and produced comparable values, but the solvents 1-2-3 were characterized by the slow rate at which the solution migrated up the chromatography strip, from 20 to 30 minutes. The solvent 4 migrated in 10 minutes. The results (mean of two paper) are shown in Table I.

In a clinical situation, the small difference in results is probably insignificant. It was observed in the same table, that with the solvent 4 the results are in agreement with the standard method.

The percentual of impurities of ^{51}Cr-EDTA samples (utilizing Whatmann 3MM paper as suport and 33% W/V aqueous solution of ammonium sulphate pH 7,5 as solvent) are shown in Table II. A reference values was determined by conventional paper electrophoresis. The Figure 1 demonstrates the linear regression obtained by the relationship between the variables.

A systematic investigation with the four different systems revelead 33% W/V aqueous solution of ammonium sulphate pH 7,5, with small development as a system which satifactoraly resolved ^{51}Cr-EDTA.

Table I

Distribution of Radioactivity on the Strip (preliminary scanning). Percentual of total Radioactivity When four Different Solvents were used

Strip Section	Solvents			
	1	2	3	4
1 (origin)	0.37	0.14	0.06	0.10
2	0.15	0.06	0.04	0.06
3	0.27	0.04	0.01	0.01
4	0.47	0.11	0.01	0.12
5	0.66	0.14	0.17	0.42
6	1.12	0.30	2.41	3.43
7	2.01	2.48	20.64	15.06
8	7.27	14.02	45.50	32.95
9	36.55	42.54	25.64	35.52
10 (solvent front)	51.03	40.11	5.48	12.29
% of the impurities	1.92	0.49	0.29	0.71

Note: The percentual of impurities obtained with the standard method (paper electrophoresis) in these experiments was 0.79 as found in the solvent 4.

Table II

Comparison of percentual values of impurities in the analysis of ^{51}Cr-EDTA samples by electrophoresis and miniaturized chromatography system with 33% W/V aqueous solution of ammonium sulphate pH 7,5 as solvent.

Samples	Percentagem of Impurities	
	Electrophoresis	Chromatography
1	0.23	0.22
2	0.88	0.81
3	0.85	0.85
4	0.55	0.49
5	0.30	0.24
6	0.17	0.18
7	0.85	0.88
8	0.27	0.28
9	0.57	0.59
10	0.23	0.24
mean value r = 9.9931	0.49	0.47

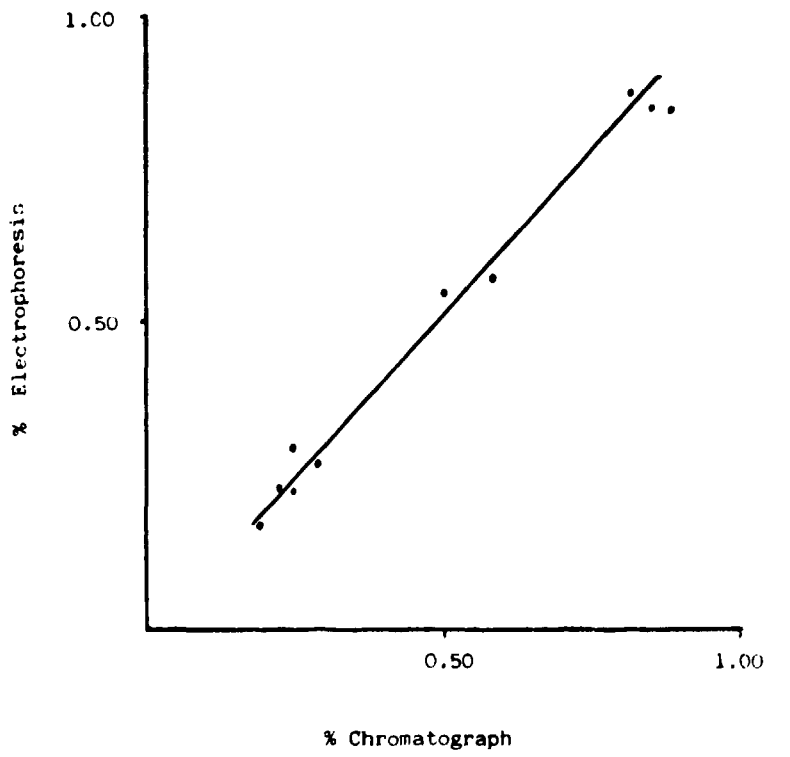

Figure 1 – Graphic Representation of Percentual Results of Impurities Electrophoresis versus Miniaturized Chromatograph for ^{51}Cr-EDTA.

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